

WHAT IS CLAIMED IS:

1. An isolated nucleic acid encoding a beta subunit polypeptide of a potassium channel, wherein the beta subunit polypeptide:

5 (i) forms, with at least one alpha subunit polypeptide, a Slo potassium channel; and  
(ii) comprises an amino acid sequence that has greater than 70% identity to the S1-S2 region of BK beta 2, BK beta 3, or BK beta 4.

10 2. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a polypeptide that specifically binds to polyclonal antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:1, SEQ ID NO: 3, or SEQ ID NO:5

15 3. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes human BK beta 2.

4. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes human BK beta 3.

20 5. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes human BK beta 4.

25 6. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a polypeptide comprising an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

7. The isolated nucleic acid sequence of claim 1, wherein the nucleic acid comprises a nucleotide sequence of SEQ ID NO:2 , SEQ ID NO:4, or SEQ ID NO:6.

30 8. The isolated nucleic acid of claim 1, wherein the nucleic acid is amplified by primers that selectively hybridize under stringent hybridization conditions to the same sequence as primers selected from the group consisting of:

5-ATGACAGCCTTTCCTGCCTCAGGGAAG-3 (SEQ ID NO:7)

5-AGATTTCTCTGCTCTTCCTTTGCTCCTCC-3 (SEQ ID NO:8)

5-GGCTGGCTGGACTGTAGAAGCATG-3 (SEQ ID NO:9)

35 5-GAGGCTGTCCAGATAAATCCCAAGTGC-3 (SEQ ID NO:10)

5-GGACTGAGAAGCCCATCATGGCAAACC-3 (SEQ ID NO:11);

5-ATGGCGAAGCTCCGGGTGGCTTAC-3 (SEQ ID NO:12)

5-TTAAGAGAACTTGCGCTTCTTCATGG-3 (SEQ ID NO:13)

5 GATGTGCTTCTGCATCGCACTCATG-3 (SEQ ID NO:14); and

5-AAGATGTGATATGGACCAGTGGCC-3 (SEQ ID NO:15)

5-TTATCTATTGATCCGTTGGATCCTCTC-3 (SEQ ID NO:16)

5-CTCCTTCAGCTGTCCTCCAGACTGC-3 (SEQ ID NO:17)

10 5-GTCCCAGTAGAATAGCTCGGTCCTC-3 (SEQ ID NO:18).

9. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a beta subunit having a molecular weight of about between 24-34 kDa.

15 10. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a beta subunit having a molecular weight of about between 18-28 kDa.

11. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a beta subunit having a molecular weight of about between 22-32 kDa.

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12. The isolated nucleic acid of claim 1, wherein the nucleic acid selectively hybridizes under moderately stringent hybridization conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

25 13. An isolated nucleic acid that specifically hybridizes under stringent conditions to a nucleic acid encoding an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:5.

30 14. A method of detecting a nucleic acid, the method comprising contacting the nucleic acid with an isolated nucleic acid of claim 13.

15. An isolated nucleic acid encoding a beta subunit polypeptide, said nucleic acid specifically hybridizing under stringent conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

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16. An isolated beta subunit polypeptide of a potassium channel, wherein the beta subunit polypeptide:

- (i) forms, with at least one alpha subunit polypeptide, a Slo potassium channel; and
- (ii) comprises an amino acid sequence that has greater than 70% identity to the S1-S2 region of BK beta 2, BK beta 3, or BK beta 4.

17. The isolated beta subunit of claim 16, wherein the polypeptide specifically binds to polyclonal antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

18. The isolated beta subunit of claim 16, wherein the polypeptide comprises an amino acid sequence of human BK beta 2.

19. The isolated beta subunit of claim 16, wherein the polypeptide comprises an amino acid sequence of human BK beta 3.

20. The isolated beta subunit of claim 16, wherein the polypeptide comprises an amino acid sequence of human BK beta 4.

21. The isolated beta subunit of claim 16, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

22. An antibody that selectively binds to the beta subunit of claim 21.

23. An expression vector comprising the nucleic acid of claim 1.

24. A host cell transfected with the vector of claim 23.

25. A method for identifying a compound that increases or decreases ion flux through a potassium channel, the method comprising the steps of:

(i) contacting the compound with a potassium channel comprising a beta subunit polypeptide, wherein the beta subunit:

(a) forms, with at least one alpha subunit polypeptide, a Slo potassium channel;

(b) comprises an amino acid sequence that has greater than 70% identity to the S1-S2 region of a BK beta 2, BK beta 3, or a BK beta 4; and

(ii) determining the functional effect of the compound upon the Slo potassium channel.

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26. The method of claim 25, wherein the functional effect is a physical effect.

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27. The method of claim 25, wherein the functional effect is a chemical effect.

28. The method of claim 25, wherein the polypeptide is expressed in a eukaryotic host cell or cell membrane.

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29. The method of claim 25, wherein the functional effect is determined by measuring changes in current or voltage.

30. The method of claim 25, wherein the beta subunit is recombinant.

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31. The method of claim 25, wherein the functional effect is determined by measuring ligand binding to the channel.

32. The method of claim 25, wherein the beta subunit comprises an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

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33. A method of detecting the presence of BK beta 2 in a sample, the method comprising the steps of:

(i) isolating a biological sample;

(ii) contacting the biological sample with a BK beta 2-specific reagent that selectively associates with BK beta 2; and,

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(iii) detecting the level of BK beta 2-specific reagent that selectively associates with the sample.

34. The method of claim 33, wherein the BK beta 2-specific reagent is selected from the group consisting of: BK beta 2-specific antibodies, BK beta 2-specific oligonucleotide primers, and BK beta 2 specific-nucleic acid probes.

5 35. The method of claim 33, wherein the sample is from a human.

36. A method of detecting the presence of BK beta 3 in a sample, the method comprising the steps of:

(i) isolating a biological sample;

10 (ii) contacting the biological sample with a BK beta 3-specific reagent that selectively associates with BK beta 3; and,

(iii) detecting the level of BK beta 3-specific reagent that selectively associates with the sample.

15 37. The method of claim 36, wherein the BK beta 3-specific reagent is selected from the group consisting of: BK beta 3-specific antibodies, BK beta 3-specific oligonucleotide primers, and BK beta 3 specific-nucleic acid probes.

38. The method of claim 36, wherein the sample is from a human.

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39 A method of detecting the presence of BK beta 4 in a sample, the method comprising the steps of:

(i) isolating a biological sample;

25 (ii) contacting the biological sample with a BK beta 4-specific reagent that selectively associates with BK beta 4; and,

(iii) detecting the level of BK beta 4-specific reagent that selectively associates with the sample.

30 40. The method of claim 39, wherein the BK beta 4-specific reagent is selected from the group consisting of: BK beta 4-specific antibodies, BK beta 4-specific oligonucleotide primers, and BK beta 4-specific nucleic acid probes.

41. The method of claim 39, wherein the sample is from a human.

42 A method for identifying a compound that increases or decreases ion flux through a potassium channel comprising a beta subunit polypeptide, the method comprising the steps of:

(i) entering into a computer system an amino acid sequence of at least 25 amino acids of a beta subunit polypeptide or at least 75 nucleotides of a nucleic acid encoding the polypeptide, the polypeptide comprising a subsequence having an amino acid sequence of SEQ ID NO:3;

(ii) generating a three-dimensional structure of the polypeptide encoded by the amino acid sequence;

(iii) generating a three-dimensional structure of the potassium channel comprising the beta subunit polypeptide;

(iv) generating a three-dimensional structure of the compound; and

(v) comparing the three-dimensional structures of the polypeptide and the compound to determine whether or not the compound binds to the polypeptide.

43. In a computer system, a method of screening for mutations of human BK beta 2, BK beta 3, or BK beta 4 genes, the method comprising the steps of:

(i) entering into the system at least about 25 nucleotides of first nucleic acid sequence encoding a beta subunit having a nucleotide sequence of SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6;

(ii) comparing the first nucleic acid sequence with a second nucleic acid sequence having substantial identity to the first nucleic acid sequence; and

(iii) identifying nucleotide differences between the first and second nucleic acid sequences.

44. The method of claim 43, wherein the second nucleic acid sequence is associated with a disease state.

45. In a computer system, a method for identifying a three-dimensional structure of BK beta 2, BK beta 3, or BK beta 4 subunits, the method comprising the steps of:

(i) entering into the system an amino acid sequence of at least 25 amino acids of a beta subunit or at least 75 nucleotides of a gene encoding the beta subunit, the beta subunit having an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5; and

(ii) generating a three-dimensional structure of the beta subunit encoded by the amino acid sequence.

46. The method of claim 45, wherein said amino acid sequence is a primary structure and wherein said generating step includes the steps of:

(i) forming a secondary structure from said primary structure using energy terms determined by the primary structure; and

(ii) forming a tertiary structure from said secondary structure using energy terms determined by said secondary structure.

47. The method of claim 46, wherein said generating step further includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

48. The method of claim 46, further comprising the step of identifying regions of the three-dimensional structure of a BK beta 2, BK beta 3 or BK beta 4 subunit that bind to ligands and using the regions to identify ligands that bind to the beta subunit.

49. A method for identifying a compound that increases or decreases ion flux through a type II BK potassium channel, the method comprising the steps of:

(i) contacting the compound with a potassium channel comprising a BK beta 3 subunit, wherein the beta subunit:

(a) forms, with at least one alpha subunit, a Slo1 potassium channel;

(b) comprises an amino acid sequence that has greater than 70% identity to the S1-S2 region of BK beta 3; and

(ii) determining the functional effect of the compound upon the Slo1 potassium channel.

50. The method of claim 49, wherein the functional effect is a physical effect.

51. The method of claim 49, wherein the functional effect is a chemical effect.

52. The method of claim 49, wherein the polypeptide is expressed in a eukaryotic host cell or cell membrane.

53. The method of claim 49, wherein the functional effect is determined by measuring ligand binding to the channel.

54. The method of claim 49, wherein the functional effect is determined by measuring changes in current or voltage.

55. The method of claim 49, wherein the BK beta 3 subunit is recombinant.

56. The method of claim 49, wherein the polypeptide has an amino acid sequence of SEQ ID NO:5.

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